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Pattern of T2 hypointensity associated with ring-enhancing brain lesions can help to differentiate pathology

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Abstract Ring-enhancing lesions seen on MR images can occur with a variety of etiologies. Some ring-enhancing lesions have hypointense rims peripherally on T2-weighted MR images. In this study, we examined whether T2 hypointense rims were associated with specific pathologies. A search for ring-enhancing lesions on MR images obtained from 1996 to 2004 was performed, and revealed 221 patients with MRI findings of ring enhancement. The pattern of T2 hypointensity (arc or rim) corresponding with ring enhancement was recorded. In addition, we analyzed other imaging characteristics, including signal on diffusion-weighted images, central homogeneity on T2 and multiplicity of lesions. We then reviewed clinical data on the patients to ascertain the diagnosis for each examination. The most common associated pathologies in our study were gliomas (40%), metastases (30%), abscesses (8%) and multiple sclerosis (MS; 6%). Hypointense borders on

T2-weighted images were present in 67% of lesions in the form of a rim in 40% and an arc in 60%. Abscesses had the highest percentage of hypointense rims. Metastases and gliomas more commonly had arcs, and MS lesions were divided between rims and arcs. Abscesses and MS lesions were more commonly homogeneous centrally, compared to gliomas and metastases. Additionally, abscesses were more often bright on diffusion imaging than the other pathologies. As expected, abscesses and MS lesions were usually multiple, whereas metastases were typically multiple in approximately 50% of the patients; gliomas were generally solitary. Trends in T2 hypointensity may aid in distinguishing among etiologies of ring-enhancing lesions, although there is overlap between the MR appearance of these various pathologies.

Keywords Ring-enhancing lesions · T2 peripheral hypointensity · Multiple sclerosis · Brain tumor · Brain abscess

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Introduction

A variety of intracranial pathologies can present as ring-enhancing lesions on MR images including metastasis, abscess, glioma, infarct, contusion, demyelinating disease, radiation necrosis and lymphoma. A ring-enhancing lesion on T1-weighted MR imaging sequences with gadolinium enhancement may have a hypointense rim on T2-weighted sequences. For clarity, we use “rim” to refer to a complete T2 hypointense border and use “ring” for gadolinium

enhancement in a complete circular border. This has most commonly been reported in abscesses where the hypointense rim is thought to result from the generation of paramagnetic free radicals by macrophages [1]. In fact, Haimes et al. found that nearly all abscesses in their study had this hypointense border between the necrotic center and peripheral edema [1]. A similar finding is present in some multiple sclerosis (MS) plaques, where a central area of high signal intensity is surrounded by a rim of lower signal intensity on T2-weighted images [2]. In other types

of pathology, such as intracranial hematomas and vascular malformations, hypointense rims are likely due to hemosiderin-laden macrophages at the lesion margins [3]. Atlas et al. found peripheral hypointensity around the majority of the intracranial malignancies they evaluated and concluded this resulted from prior tumor hemorrhage [4]. However, this was usually a “broken” rim rather than a complete rim (which was observed in only 1 of 15 patients). Other authors have proposed that in granulomatous disease occasional T2 hypointensity may be present peripherally due to a fibrous rim of granulation tissue and compressed glial tissue [5].

Despite papers describing peripheral hypointensity associated with certain pathologies, the overall prevalence of T2 hypointense borders in ring-enhancing lesions has not been reported. Additionally, the significance of this finding, specifically in distinguishing among different etiologies of ring-enhancing lesions, has not been explored. Researchers have used a variety of other methods to aid in distinguishing among ring-enhancing lesions. Authors have indicated that diffusion-weighted (DW) MR imaging may be helpful in cases of cerebral ring-enhancing masses, specifically necrotic tumors and abscesses [6]. Abscesses generally demonstrate high signal on heavily diffusion-weighted images as well as low signal and ADC values on ADC maps. The opposite findings are usually true for necrotic or cystic tumors [6–9]. While these techniques are becoming more widely used in practice, they are not universally accepted. A study by Ray et al. [10] demonstrated that nuclear imaging helped differentiate between neoplastic and non-neoplastic conditions in 42% of their patients where CT or MRI were doubtful. Additional findings on MRI can also help distinguish between infectious and neoplastic etiologies. For example, communication with the ventricular system and meningeal and ependymal enhancement are more suggestive of cerebral abscess [11].

The goals of this study were to document the presence of T2 hypointense borders in ring-enhancing lesions of various etiologies, to determine the prevalence of this finding in ring-enhancing lesions and to analyze whether this finding assists in distinguishing between different pathologies. Additionally, we noted other imaging characteristics of these lesions to determine if a constellation of imaging findings, including peripheral T2 hypointensity, was useful for distinguishing among etiologies.

Methods

Patients

Following Institutional Review Board approval, the radiology report database at our institution was searched for MR images of the head with gadolinium enhancement performed from January 1996 to May 2004. This subset of reports was then

searched for “ring-enhanc*”, “peripheral enhanc*” and “centrally necro*” where “*” was a wild-card allowing matching of any subsequent character(s). This search revealed 608 examinations meeting these criteria. Each MRI examination was reviewed by an investigator blinded to the patient’s diagnosis to confirm that it met the following additional criteria. Examinations were excluded for the following reasons: non-parenchymal lesion; lesions with minimal or partial ring enhancement on T1-weighted images with gadolinium; ring enhancement due to recent surgery; more than one examination in a single patient; necessary sequences not performed (axial T1 with gadolinium and axial T2 were required); MR images not available for review; lesions too small or subtle to evaluate; or diagnosis unknown. Only lesions with a complete ring of enhancement on T1 with gadolinium were included. Additionally, reports in the search which contained wording such as “no ring-enhancing lesions” or “ring-enhancing lesions have resolved” were excluded. In cases where there were more than one examination in a patient, the images from their earliest MRI were evaluated. Of the original 608 examinations, 387 were excluded for these reasons, leaving 221 studies.

MR image analysis

The T1-weighted images with gadolinium were reviewed. If more than one ring-enhancing lesion was present, the largest lesion was evaluated on all of the imaging slices on which it appeared. This lesion was reviewed on the T2-weighted images to determine whether a relatively hypointense border was present compared to the surrounding edema and lesion center. The lesions with surrounding hypointensity on T2 were then categorized as having an arc (part of the lesion border) or rim (all of the lesion border) of hypointensity. Of these MR images, 10% were reviewed by a second blinded investigator to assess the reproducibility of categorization.

Although the focus of the study was on peripheral T2 hypointensity, some additional data were collected. The center of each lesion was assessed on T2-weighted images to determine whether it was homogeneous or heterogeneous. DW imaging was evaluated, if available. Each lesion was determined to be bright, dark or mixed (areas of bright and dark) on DW images.

Correlation with pathology

After image categorization, pathology results and clinical information were obtained from patient records. The relationship between T2 hypointensity and pathology was assessed. In 69% of patients (153), there was pathologic proof of the diagnosis. In the remaining 31% (68), the diagnosis was made by clinical history, laboratory evaluation and/or radiologic examination. For example, the diagnosis of MS was usually based on patient history,

physical examination and MR imaging. Patients with brain metastases did not always have the brain lesion biopsied if they had biopsy-proven cancer elsewhere.

Diagnoses were organized into the following categories: abscess, glioma, infarct, lymphoma, metastasis, demyelinating disease, non-bacterial infection, other non-brain tumor, other tumor, radiation necrosis, and miscellaneous.

Statistical analysis

Statistical analysis was performed comparing the largest four groups of pathology: abscess, glioma, metastasis and MS. The Fisher's exact test (F-E) was performed when two variables were present. The Kruskal-Wallis test (K-W) was used when three ordered variables were present. When paired comparisons were employed, the Bonferroni correction was applied; therefore, statistical significance was present at $P < 0.008$ for these specific comparisons. For the remaining analyses, statistical significance was considered present at $P < 0.05$.

Results

Pathology of ring-enhancing lesions

The most prevalent pathologies associated with ring-enhancing lesions were gliomas (40%) and metastases (30%), followed by abscesses (8%) and MS lesions (6%). The remaining 16% of pathologies included infarcts, lymphoma, non-bacterial, other non-brain tumors, other tumors, radiation necrosis, and miscellaneous. The non-bacterial ring-enhancing lesions included lesions due to aspergillosis, cryptococcus, histoplasmosis, progressive multifocal leukoencephalopathy (PML), tuberculosis and toxoplasmosis. Other non-brain tumors were an arachnoid cyst, a hemangioma, meningiomas and a skull-based squamous cell carcinoma with intraparenchymal extension. Other tumors included a dysembryoplastic neuroepithelial tumor (DNET), a primitive neuroectodermal tumor (PNET) and a medulloblastoma. Intraparenchymal hemorrhage, leukoencephalopathy and scar tissue were categorized as miscellaneous.

T2 hypointensity

Hypointense borders were present on T2-weighted images in 67% of the ring-enhancing lesions in our study (Table 1). Of these lesions, a hypointense rim was present in 40% and the remaining 60% had a hypointense arc. Abscesses had the highest percentage of hypointense borders (89% of lesions), with 75% of these being hypointense rims and 25% hypointense arcs. Of the gliomas, 69% had hypointense borders, of which 26% were rims and 74% arcs.

Table 1 Number (and percent) of each pathology type with the given MR characteristics

	Abscess	Glioma	Infarct	Lymphoma	Metastases	MS lesions	Non-bacterial tumor	Other non-brain tumor	Other tumor	Radiation necrosis	Miscellaneous
Total	18 (8%)	88 (40%)	3 (1%)	5 (2%)	67 (30%)	13 (6%)	9 (4%)	6 (3%)	3 (1%)	5 (2%)	4 (2%)
hypointensity on T2	16 (89%)	61 (69%)	1 (33%)	5 (100%)	45 (67%)	7 (54%)	3 (33%)	4 (67%)	3 (100%)	2 (40%)	2 (50%)
Rim	12 (75%)	16 (26%)	1 (100%)	4 (80%)	14 (31%)	4 (57%)	3 (100%)	2 (40%)	0 (NA)	1 (50%)	2 (100%)
Arc	4 (25%)	45 (74%)	0 (NA)	1 (20%)	31 (69%)	3 (43%)	0 (NA)	2 (40%)	3 (100%)	1 (50%)	0 (NA)
No hypointensity	2 (11%)	27 (31%)	2 (67%)	0 (NA)	22 (33%)	6 (46%)	6 (67%)	2 (33%)	0 (NA)	3 (60%)	2 (50%)
Multiplicity of lesions											
Multiple	13 (72%)	20 (23%)	1 (33%)	4 (80%)	37 (55%)	11 (85%)	2 (22%)	0 (NA)	2 (67%)	2 (40%)	1 (25%)
Single	5 (28%)	68 (77%)	2 (67%)	1 (20%)	30 (45%)	2 (15%)	7 (78%)	6 (100%)	1 (33%)	3 (60%)	3 (75%)
Center homogeneity ^a											
Homogeneous	10 (56%)	12 (14%)	1 (33%)	1 (20%)	20 (30%)	12 (92%)	0 (NA)	1 (17%)	1 (33%)	1 (20%)	0 (NA)
Heterogeneous	8 (44%)	74 (84%)	2 (67%)	4 (80%)	47 (70%)	1 (8%)	9 (100%)	5 (83%)	2 (67%)	4 (80%)	4 (100%)
Diffusion ^a	10 (56%)	16 (18%)	2 (67%)	1 (20%)	15 (22%)	3 (23%)	4 (44%)	0 (NA)	0 (NA)	1 (20%)	3 (75%)
Bright	7 (70%)	2 (13%)	1 (50%)	0 (NA)	0 (NA)	1 (33%)	1 (25%)	0 (NA)	0 (NA)	0 (NA)	0 (NA)
Dark	2 (20%)	3 (19%)	1 (50%)	0 (NA)	4 (6%)	0 (NA)	2 (50%)	0 (NA)	0 (NA)	1 (100%)	1 (25%)
Mixed	1 (10%)	9 (56%)	0 (NA)	1 (100%)	11 (16%)	2 (67%)	1 (25%)	0 (NA)	0 (NA)	0 (NA)	2 (50%)

^aTwo gliomas were too small to characterize the center or diffusion

Metastases had a similar distribution with 68% having hypointense borders, of which 30% were rims and 70% arcs. Of the MS lesions, 54% had hypointense borders fairly evenly divided between rims (57%) and arcs (43%). There was no statistically significant difference between the prevalence of hypointense borders in abscesses, gliomas, metastases and MS lesions (F-E, $P=0.17$). The number of lesions in the other categories was too small for statistical analysis.

There was, however, a significant difference between the distribution of arcs and rims among the four main groups of pathology (K-W, $P=0.0035$). On paired comparison, abscesses and gliomas were different (K-W, $P=0.0003$), with abscesses more likely to have hypointense rims and gliomas more likely to have hypointense arcs. A difference also existed between abscesses and metastases (K-W, $P=0.0005$), with metastases more commonly having hypointense arcs. No significant difference was present between abscesses and MS lesions, with MS lesions evenly divided between arcs and rims. Gliomas and metastases had similar findings (K-W, $P>0.99$). Glioma versus MS lesions and metastases versus MS lesions were not different, which is most likely a consequence of the smaller MS sample size.

Comparing the location of the enhancing ring on T1-weighted images with gadolinium to the hypointense border (rim or arc) on T2-weighted images, a significant difference was found between the groups (K-W, $P=0.01$). Specifically, the hyperintense ring and hypointense border were likely to correspond to the same location in abscesses, whereas in gliomas only part of the T1 ring and T2 border corresponded (K-W, $P=0.001$). No other significant differences existed between groups with paired comparison. Metastases were again similar to glioma in that the majority of lesions had correspondence between part of the T1 ring and the T2 border. MS lesions were divided between partial and complete correspondence.

Homogeneity of lesion center

The homogeneity of the central portion of each lesion was evaluated on T2-weighted images. On T2, 27% of lesions had homogeneously increased signal centrally, while the rest were centrally heterogeneous (Table 2). Abscesses were divided between homogeneous (56%) and heterogeneous (44%) centers. Heterogeneous centers were most prevalent in gliomas (84%) and metastases (70%). Nearly all MS lesions were homogeneous centrally (92%, Table 2). A significant difference existed between these groups (F-E, $P<0.0001$). Abscesses were more likely than gliomas to be homogeneous on T2 (F-E, $P=0.0004$). MS lesions were more likely to be homogeneous than gliomas (F-E, $P<0.0001$) and metastases (F-E, $P<0.0001$). No significant difference existed between abscesses and metastases (F-E, $P=0.05$), abscesses and MS lesions (F-E, $P=0.04$), or gliomas and metastases (F-E, $P=0.03$) using $P<0.008$ for these paired comparisons as described in the Methods section.

Diffusion

DW imaging was only performed in 25% of examinations included in this study. Abscesses were the most likely to have DW imaging (56%) compared to 18% of gliomas, 22% of metastases and 23% of MS lesions (F-E, $P=0.01$), likely reflecting clinical suspicion. A significant difference existed in signal characteristics on DW images among pathologies (K-W, $P=0.03$). Abscesses were much more often bright on DW images (70%) compared to gliomas (13%), metastases (0%) and MS lesions (33%). However, this difference was only statistically significant when comparing abscesses and metastases, which were more often mixed on DW images (K-W, $P=0.0003$). The P -value comparing abscess and glioma, most often mixed on DW

Table 2 Prevalence of peripheral hypointensity, central homogeneity, increased signal on DW images and multiplicity of lesions among all of the lesions in the study

MR findings	Number of studies	Percentage of lesions
Hypointense border on T2	149	67%
Rim	59	39% of those with hypointense borders
Arc	92	61% of those with hypointense borders
No hypointensity	72	33%
Center homogeneity ^a		
Homogeneous	59	27%
Heterogeneous	160	73%
DW imaging performed ^a	55	25%
Bright	12	23% of those with DWI performed
Mixed (dark and bright)	27	51% of those with DWI performed
Dark	14	26% of those with DWI performed
Multiplicity of lesions		
Multiple	93	42%
Single	131	58%

^aTwo lesions (gliomas) were too small to characterize the center or diffusion characteristics

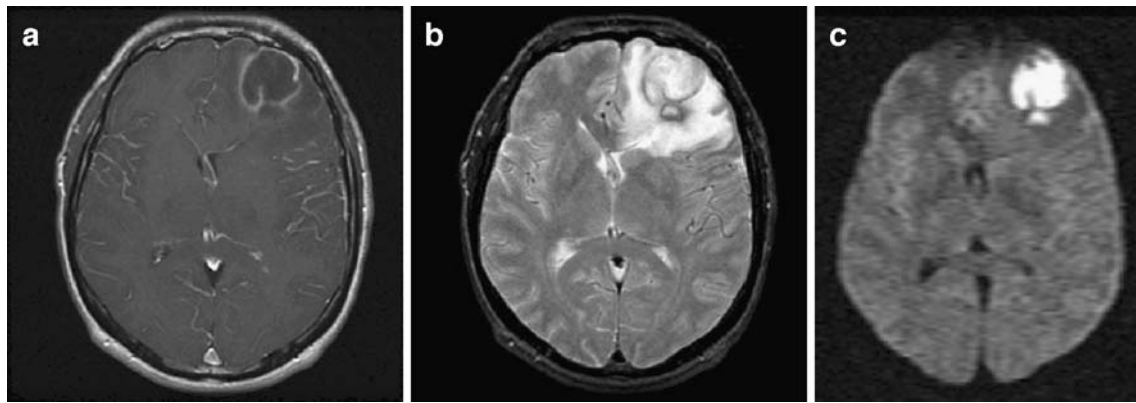


Fig. 1 **a** Ring-enhancing abscess seen on T1-weighted MR with gadolinium. **b** On T2-weighted MR imaging, this abscess demonstrates a hypointense peripheral rim between the central portion of the abscess and the surrounding peripheral edema, the

most common appearance of abscesses in the study. The center of the lesion is somewhat heterogeneous. **c** DW imaging of this abscess demonstrates a bright signal

images, was suggestive of a difference ($P=0.04$). Differences between the other groups were not significant.

these 23 lesions, there was 100% agreement between investigators.

Multiplicity of lesions

Abscesses and MS lesions were more often multiple (72% and 85%, respectively) than gliomas (23%), as expected. Among the metastases 55% were multiple (Table 1). The differences between abscesses and gliomas (F-E, $P=0.0001$), gliomas and metastases (F-E, $P<0.0001$) and gliomas and MS lesions (F-E, $P=0.0001$) were statistically significant.

Reproducibility of results

As mentioned in the Methods section, 10% of the lesions were randomly selected and reviewed by a second investigator blinded to the interpretation of the first investigator. For

Discussion

Peripheral hypointensity on T2-weighted images has been described in a variety of lesions, but the specificity of this finding has not been reported. In this study, we found that hypointensity corresponding with ring-enhancement was frequently encountered in abscesses, gliomas, metastases and MS lesions, and that there were definite trends that distinguish these diagnoses. The histologic correlate of this hypointense rim in each of these pathologies is unclear, but it may correspond to the paramagnetic free radicals produced by macrophages, hemosiderin-containing macrophages or a fibrous rim. Additionally, although the other pathologic categories were too small to analyze statistically, hypointense borders could be found on T2-weighted

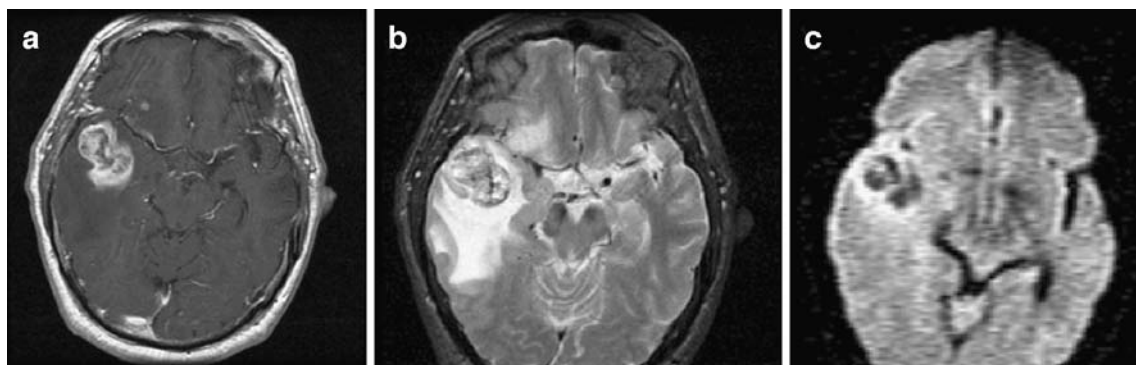


Fig. 2 **a** Glioma (glioblastoma multiforme) with ring-enhancement on T1-weighted MR imaging with gadolinium. **b** On T2-weighted MR imaging, this glioma demonstrates a peripheral arc of hypointensity, seen medially. The center of the lesion is heterogeneous on this MR sequence. **c** DW imaging shows a mixed signal

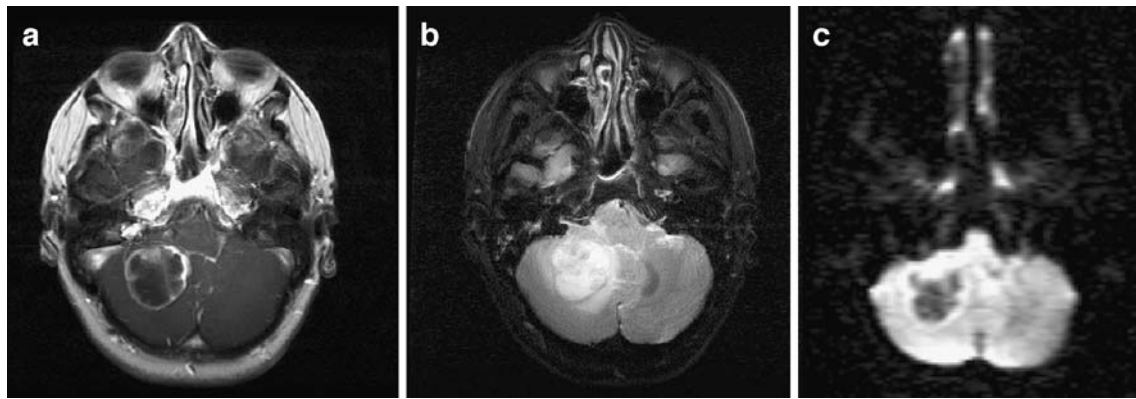


Fig. 3 **a** Metastatic non-small-cell lung cancer as ring-enhancing lesion in the right cerebellum on T1-weighted MR imaging with gadolinium. **b** Hypointense arc on T2-weighted image, seen

posteriorly. The center of this lesion is heterogeneous. **c** DW imaging shows a mixed signal

images in infarcts, lymphoma, non-bacterial infections (aspergillosis, PML and toxoplasmosis), miscellaneous lesions (intraparenchymal hemorrhage and scar tissue), non-intraparenchymal lesions (arachnoid cyst, hemangioma, meningioma and skull-based squamous cell carcinoma with temporal lobe invasion), other tumors (DNET, PNET and medulloblastoma), and radiation necrosis. Thus, a T2 hypointense border is not specific to any one etiology of ring-enhancing lesions. However, it is unusual for some of these entities to show enhancement (for example, DNET, PML and leukoencephalopathy), so these pathologies are not generally included in the differential of ring-enhancing lesions.

Differences did exist, however, in the frequency of hypointensity and the shape it took among the lesions. Abscesses most commonly had complete hypointense rims on T2-weighted images (Fig. 1). Frequently, the entirety of this hypointense rim corresponded to the same location as the hyperintense ring on T1-weighted gadolinium-enhanced images. Approximately two-thirds of gliomas demonstrated peripheral hypointensity as well, although the majority of gliomas had arcs that only partly cor-

responded to the enhancing ring (Fig. 2). Metastases had very similar findings to gliomas, with peripheral arcs most commonly demonstrated on T2-weighted imaging (Fig. 3). Only half of the MS lesions in our study had peripheral hypointensity, which was evenly divided between arcs and rims (Fig. 4). The orientation of the hypointense arc was not investigated in this study, but may be a valuable assessment in future research. For example, Masdeu et al. found that MS lesions are often ring-enhancing arcs on T1-weighted images with gadolinium, and the open portion of the ring generally abuts the gray matter of the cortex or basal ganglia [12]. It therefore follows that the orientation of hypointense arcs on T2-weighted images may vary among pathologies.

In addition to peripheral hypointensity, other MRI features were different between pathologies. On T2, MS lesions were almost all homogeneous centrally, while abscesses were more evenly divided between homogeneous and heterogeneous. Gliomas and metastases, however, were more often heterogeneous centrally. Also, the majority of abscesses were bright on diffusion, as expected from prior studies. Gliomas and metastases were often

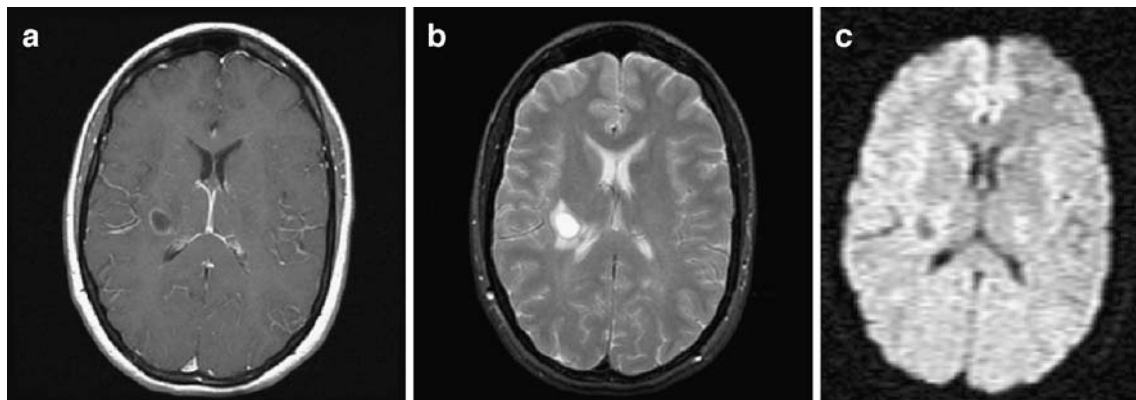


Fig. 4 **a** MS lesion with ring-enhancement on T1-weighted MR imaging with gadolinium. **b** This lesion has a peripheral hypointense rim and is homogeneous centrally on T2-weighted MR imaging. **c** DW imaging shows a mixed, although mostly dark, signal

mixed, with regions of bright and dark on DW images. MS lesions were of variable signal on DW images, likely corresponding to different ages of the lesions, though a particular lesion is likely to be homogeneous. However, since analysis of DW images was not a central part of the study, the ADC maps were not evaluated to differentiate T2 shine-through from true restricted diffusion. Not surprisingly, abscesses and MS lesions were often multiple, metastases were equally solitary or multiple and gliomas were usually solitary lesions.

From these trends, it can be inferred that a ring-enhancing lesion with a hypointense rim on T2 and bright signal on diffusion is most likely an abscess, especially if other lesions are present. A lesion with a hypointense arc on T2 and heterogeneous center is likely a neoplasm, either a glioma or a metastasis. A metastasis is more probable than a glioma if multiple lesions are present. Ring enhancement with a homogeneous center and multiple lesions may be a MS lesion or abscess, but a MS lesion is more likely if the lesion is dark or mixed on DW images.

Despite these trends, significant overlap exists between the appearance of ring-enhancing lesions on MR images. This may reflect the nonspecific nature of the hypointensity, which can be seen with paramagnetic free radicals produced by macrophages, hemosiderin within macrophages or even marginal vessels. Additionally, some authors have suggested that hypointensity may change over time, even resolving in certain pathologies after treatment [1]. Therefore, lesion evolution may influence whether or not peripheral hypointensity is present. Clinical history and serial examinations are often necessary to arrive at the correct etiology. However, the characteristics described above may aid in narrowing and prioritizing the differential diagnosis of these lesions.

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